polymorphisms in the survivin gene by direct sequencing of genomic DNA samples from 27 healthy Koreans, and then performed a case-control study to evaluate the association of the polymorphisms with lung cancer risk. The survivin genotypes were determined by PCR amplification and melting curve analysis in 582 lung cancer patients and in 582 healthy controls. We identified 8 single nucleotide polymorphisms (SNPs): 6 known SNPs [-644T>C, -625G>C, -31C>G, 9194A>G (K129E), 9386T>C and 9809T>C] and 2 novel SNPs (9974C>T and 10347G>A). Among the SNPs studied, the -31C>G genotype distribution was significantly different between the cases and controls (P = 0.04). Individuals with at least one -31G allele were at a significantly decreased risk of lung cancer compared to those individuals with the -31CC genotype (OR = 0.74, 95% CI = 0.57-0.96, P = 0.02). When the lung cancer cases were categorized by tumor histology, the -31G allele was associated with a significantly decreased risk of adenocarcinoma (OR = 0.59, 95% CI = 0.41-0.84, P = 0.003). Consistent with the results of the genotyping analysis, the -625G/-31G/9194A/9809T haplotype carrying the -31G allele was associated with a significantly decreased risk of adenocarcinoma (OR = 0.56, 95% CI = 0.40-0.77, P = 0.0004). The promoter assay revealed the -31G allele to have a significantly lower promoter activity than the -31C allele. These results suggest that the survivin -31C>G polymorphism influences survivin expression, thus contributing to the genetic susceptibility to lung cancer.

PD1-1-7 **Epidemiology and Prevention & Early Detection, Mon, 16:00 - 17:30**

Primary synchronous lung cancer detected using autofluorescence bronchoscopy

Kim, Ju Ock[1] Kwon, Sun Jung[2] Lee, Yu-Jin[1] Joung, Mi-Kyong[1] Lee, Jeong Eun[1] Park, Hee Sun[1] Jung, Sung Soo[1] Kim, Sun Young[1]

[1] Department of Internal Medicine, Chungnam National University Hospital and Cancer Research Institute, Daejeon, Korea [2] Daejeon Military Hospital, Daejeon, Korea

Background: Patients with lung cancer have a relative high risk of developing secondary primary lung cancers. This study examined the additional value of autofluorescence bronchoscopy (AFB) for diagnosing synchronous lung cancers and premalignant lesions.

Methods: Patients diagnosed with lung cancer from January 2005 to December 2005 were enrolled in this study. The patients underwent a lung cancer evaluation, which included white light bronchoscopy (WLB), followed by AFB. In addition to the primary lesions, any abnormal or suspicious lesions detected during WLB and AFB were biopsied.

Results: Seventy-six patients had non-small cell lung cancer (NSCLC) and 23 had small cell lung cancer (SCLC). In addition to the primary lesions, 84 endobronchial biopsies were performed in 46 patients. Five definite synchronous cancerous lesions were detected in three patients with initial unresectable NSCLC and in one with SCLC. The secondary malignant lesions found in two patients were considered metastatic because of the presence of mediastinal nodes or systemic involvement. One patient with an unresectable NSCLC, two with a resectable NSCLC, and one with SCLC had severe dysplasia. The detection rate for cancerous lesions by the clinician was 6.0% (6/99) including AFB compared with 3.0% (3/99) with WLB alone. The prevalence of definite synchronized cancer was 4.0% (4/99) after using AFB compared with 2.0% (2/99) before, and the staging-up effect was 1.0% (1/99) after AFB. Since the majority of patients were diagnosed with advanced disease, the subjects with newly detected cancerous lesions did not have their treatment plans altered, except for one patient with a stage-up IV NSCLC who did not undergo radiotherapy.

Conclusions: Additional AFB is effective in detecting early secondary cancerous lesions and is a more precise tool in the staging workup of patients with primary lung cancer than with WLB alone.

PD1-1-8 **Epidemiology and Prevention & Early Detection, Mon, 16:00 - 17:30**

Detection of epidermal growth factor receptor mutations from serum free DNA of non-small lung cancer patients

Han, Sle Gi Lo[1] Jung, Hae-Yun[1,2] Whang, Young Mi[1] Seo, Hee Yun[3] Sung, Hwa Jung[3] Choi, In Keun[3] Oh, Sang Cheul[3] Seo, Jae Hong[3] Shin, Sang-Won[3] Kim, Jun Suk[2,3] Kim, Yeul Hong[1,2,3]

[1] Genomic Research Center for Lung and Breast/ovarian Cancers, Seoul, Korea [2] Department of Internal Medicine and Brain Korea 21 Program for Biomedical Sciences, Seoul, Korea [3] Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

The epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, gefitinib (Iressa), was applied for the treatment of non-small lung cancer (NSCLC). Recently, EGFR mutations have known to be correlated with clinical response in gefitinib treatment. However, detection of EGFR mutations in tumor tissue has variable limitations, such as that biopsy procedure is invasive, the amount of clinical sample is limited, and many normal cells could be contaminated during tumor tissue dissection which could generate false negative results. It was well known that serum free DNA of cancer patients represents genetic changes of primary tumors. To evaluate the clinical implication of simple and sensitive detection method of EGFR mutation using serum free DNA, we examined the EGFR exon 19 and 21 mutation status in serum DNA from gefitinib treated NSCLC patients using direct sequencing and mutant enriched PCR analysis. Direct sequencing method detected EGFR mutation only in 1 patient from total 30 patients (3.3 %). This result revealed that direct sequencing method is not suitable for detection of low copy number of EGFR mutation from serum DNA. However, mutant enriched PCR analysis detected EGFR mutations in 25 patients (50%) from total 50 patients. Mutant enriched PCR method detected exon 19 mutations in 12 patients (24%), exon 21 mutations in 13 patients (26%), and both mutations in 1 patients (2%). Out of 8 patients who had partial responses (PR) with gefitinib treatment, EGFR mutations were noted in 6 patients (75%). Five out of 11 patients (45%) with stable disease (SD) showed EGFR mutations. Out of 27 patients with progressive disease (PD), EGFR mutations were detected in 13 patients (48%). To confirm the results of the mutant enriched PCR analysis, the second PCR products were directly sequenced for both exons. In result, mutant enriched PCR analysis coincided with direct sequencing analysis in exon 21. In summary, we applied 2 different EGFR mutation detection methods using serum free DNA from gefitinib treated patients. Mutant enriched PCR analysis is more specificity and sensitivity than direct sequencing. Our data showed correlation with EGFR mutation status using mutant enriched PCR method using serum free DNA and clinical gefitinib responses. The EGFR mutation status in serum free DNA might be a convenient and useful biomarker for the prediction of clinical response in gefitinib-treated NSCLC patient.

This study was supported by a grant of the Korea Health 21 R&D project, the Ministry of Health & Welfare, Republic of Korea. (A010250)